

Remarks

Applicants have amended Claims 1, 4, and 7 without prejudice or disclaimer in an effort to expedite prosecution. Claims 11-13, 17, and 19-21 were subject to a Restriction Requirement and withdrawn from consideration. Claims 9-10, 14-16 and 18 are canceled. Following entry of the above amendment, Claims 1-8 remain pending.

I. Claim rejections under 35 U.S.C § 112

Claims 1-8 were rejected under 35 U.S.C § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Office Action stated that the claim term "derivative(s)" was unclear. Applicants submit that the term "derivatives" is sufficient clear to one of skill in the art. On page 10, lines 31 - 38 of the application, it is stated that:

"Derivatives of the compounds of formula (I) include pharmaceutically acceptable derivatives. The invention is described using the following definitions unless otherwise indicated. The term "pharmaceutically acceptable derivative" means any pharmaceutically acceptable salt, ester, salt of such ester or solvate of the compounds of formula (I), or any other compound which upon administration to the recipient is capable of providing (directly or indirectly) a compound of formula (I). It will be appreciated by those skilled in the art that the compounds of formula (I) may be modified to provide pharmaceutically acceptable derivatives thereof at any of the functional groups in the compounds, and that the compounds of formula (I) may be derivatised at more than one position."

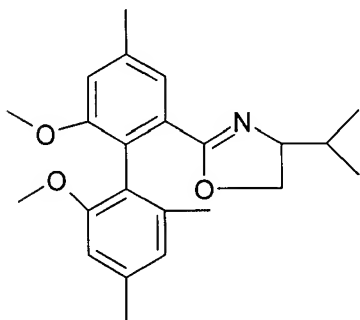
Nevertheless, applicants have amended independent Claims 1 and 4 to remove all recitations of the term, "derivative(s)" and effectively mooted the rejection of Claims 1 and 4 (and, therefore, dependant Claims 2-3 and 5-7).

Claim 7 was rejected under 35 U.S.C § 112, second paragraph as being incomplete for omitting essential elements, namely the chemical names of Examples 1-90. Applicants have amended Claim 7 to recite the chemical names for the compounds of Examples 1-90. Applicants wish to thank the Examiner for the suggested amendment.

Applicants respectfully submit that amended Claims 1-8 are definite and complete and request favorable reconsideration of the rejections under 35 U.S.C § 112.

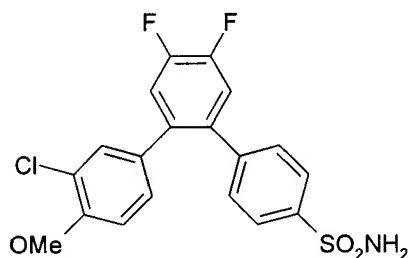
II. Claim rejections under 35 U.S.C § 102(b)

a) Claim 1 was rejected under 35 U.S.C. §102(b) as allegedly anticipated by Baker, *et al.*, *Tetrahedron letters* 1999, 40, 3475-3478 ("Baker"). The Office Action stated that on page 3475, Baker discloses the following compound (compound #4):



The Office Action also stated that Claim 1 of the present application recites where Z-Rx can be OMe and that Compound 4 contains an OMe substituent at the equivalent Z-Rx position. Applicants submit that Compound 4 of Baker does not contain an OMe substituent at the equivalent Z position. Thus, Z (and therefore Rx) is absent in Compound 4, but is required by Claims 1 and 4 of the instant application. Compound 4 contains a methyl group at the Z position while Claim 1 requires Z to be chosen from O, S, SO, or SO₂. Therefore, Compound 4 of Baker is not encompassed by amended Claims 1 and 4. Applicants respectfully submit that Claims 1-8 are patentably distinct from compound 4 of the Baker reference; and therefore, request favorable reconsideration of this rejection.

b) Claims 1-8 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by PCT Application No. WO 96/16934 to Reitz, *et al.*, ("Reitz"). The Office Action stated that Reitz discloses the following compound (compound 20) which is a "derivative" of the compounds claimed in the instant Claims 1-7:



Applicants submit that Reitz's compound 20 is not a "derivative" because it does not fall under the definition of "derivative" provided in the present application. However, in the interest of advancing prosecution, applicants have amended Claims 1 and 4 to remove the term "derivative". Applicants believe this amendment effectively moots Examiner's rejection.

Applicants respectfully submit that amended Claims 1-8 are patentably distinct from compound 20 of Reitz; and therefore, request favorable reconsideration of this rejection under 35 U.S.C. §102(b).

III. Claim rejections under 35 U.S.C § 103

Claims 1-3 and 8 were rejected under 35 U.S.C. §103 as allegedly obvious in light of PCT Application No. WO 96/16934 to Reitz, *et al.*, ("Reitz"). In explaining the basis for its obviousness rejection, the Office Action states that the difference between the Applicant's compounds and compound 20 of Reitz is the placement of substituents around a ring and that such differences are not patentable absent unexpected results.

Applicants believe that the amendments to Claims 1, 4 and 7 renders the Office Action's rejection moot. However, Applicants will address the rejections to the original claims in light of the new amendments.

Applicants respectfully submit that the Office Action fails to establish a *prima facie* case of obviousness. To establish a *prima facie* case of obviousness, the Patent Office must satisfy three criteria (MPEP 2143). First, the prior art relied upon, coupled with the knowledge generally available in the art at the time of invention, must contain some suggestion or incentive that would have motivated the skilled artisan to modify the reference. Secondly, the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. Thirdly, the prior art reference must teach or suggest all the limitations of the claims.

Regarding Claim 1, Reitz's compound 20 fails to disclose or suggest, *inter alia*, the following differences:

1. Z (and therefore Rx) is absent from compound 20. At best, the Z equivalent in compound 20 is in the para position, while the presently claimed Z is in the ortho position.
2. Rx is now aryl, heterocyclyl, or bicyclic heterocyclyl, while compound 20 shows a methyl group for the Rx equivalent.

3. Compound 20 is described by Reitz as a Cox-2 *enzyme* inhibitor showing an ID₅₀ for Cox-2 inhibition that was <0.1 μ M (page 120 of Reitz), while Applicant's exemplified compounds are EP-1 *receptor* antagonists having an IC₅₀ of between 1 μ M and 0.1 mM (page 91 of Application).

First, Reitz fails to suggest that one of skill in the art would be motivated to design a selective EP-1 receptor antagonist by adding an aryl, heterocyclyl, or bicyclic heterocyclyl group to one of the phenyl groups of Reitz's Cox-2 inhibitors. The prior art, not applicant's disclosure, must teach, suggest, or provide an incentive to make the claimed compound. See *In re Dow Chemical Co. v. American Cyanamide Co.*, 837 F.2d 469, 5 USPQ 1529 (Fed Cir. 1987). Second, there is no reasonable expectation in Reitz that adding an additional aryl, heterocyclyl, or bicyclic heterocyclyl group to one of the compound 20 phenyl groups would result in a successful EP-1 antagonist. Third, Reitz fails to teach or suggest all the limitations in Applicants' Claims 1 and 4, because no compounds were specifically described or synthesized, which have an additional ring structure other than the 3 core phenyl rings. In sum, Applicants have not merely "changed the placement of substituents around a ring" as recited in the Office Action. Instead, Applicants have added a completely unobvious ring structure to arrive at their EP-1 receptor antagonists.

Applicants respectfully submit that the Office Action fails to establish a *prima facie* case of obviousness and that Claims 1-8 are patentable over Reitz. Not only does Reitz fail to teach or suggest all the limitations of the claims, there is no motivation to modify the prior reference, and there is no motivation of success. Withdrawal of this rejection, is therefore, respectfully requested.

IV. Obviousness-type double patenting rejections

Claims 1-8 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1-3 and 5 of U.S. Patent Application No. 11/568573 ('573). The Office Action stated that conflicting Claims 1-3 and 5 (of the '573 patent) are obvious in light of Applicant's claimed invention.

MPEP section 804, Part I, subpart B1 states:

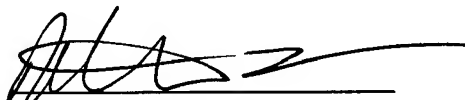
"If a "provisional" nonstatutory obviousness-type double patenting (ODP) rejection is the only rejection remaining in the earlier filed of the two pending applications, while the later-

filed application is rejectable on other grounds, the examiner should withdraw that rejection and permit the earlier-filed application to issue as a patent without a terminal disclaimer."

Applicants submit that the present application is the *earlier* filed application based on a filing date of April 28, 2005. The '573 application is the *later* filed application based on a filing date of January 18, 2006. Accordingly, Applicants believe that the Office should delay this provisional double patenting rejection until the remaining rejections have been resolved, and then withdraw the provisional double patenting and permit this application to issue as a patent without a terminal disclaimer.

Applicants believe the present claims are in condition for allowance and such action is respectfully requested. If the Examiner has any outstanding issues with the pending claims, he is encouraged to telephone the undersigned at (919) 483-8406 for expeditious handling.

Respectfully submitted,



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